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LOW-FREQUENCY HARMONIC ACCELERATION AS A TEST OF LABYRINTHINE F--ETC(U)

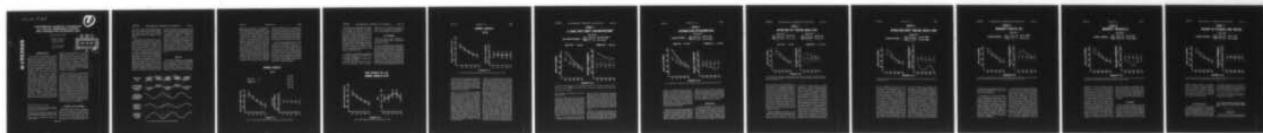
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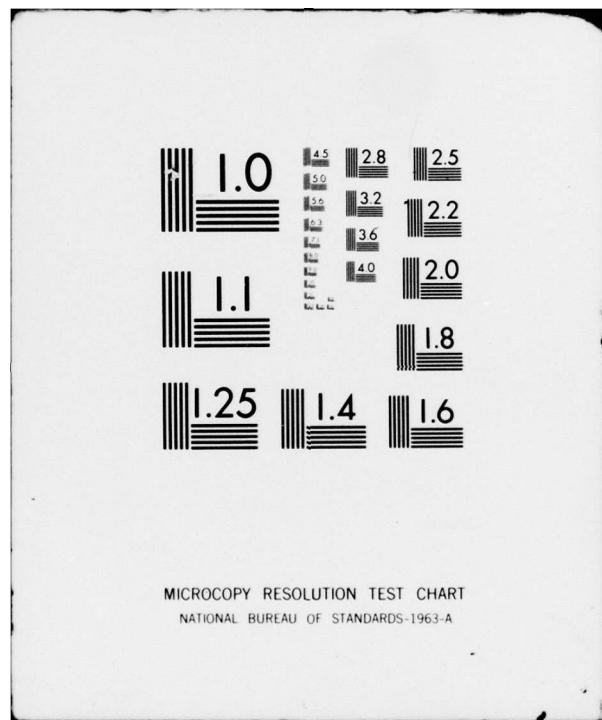
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LOW-FREQUENCY HARMONIC ACCELERATION AS A TEST OF LABYRINTHINE FUNCTION: BASIC METHODS AND ILLUSTRATIVE CASES

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INTRODUCTION

SINCE the early work of Bárány,¹ a great deal of effort has been expended in attempting to quantify the stimulus-response relationships for vestibular stimulation. Most clinical research studies have been seriously hampered by the inability to control and quantify the stimulus; this has been especially true where thermal changes within the canals have been employed (ie, water or air calorics). Furthermore, recent evidence² implies that "caloric" stimulation is a nonphysiologic stimulus and leads to differential nystagmic eye movements. Caloric testing is also confounded by the fact that alertness (which is difficult to control) plays a major role in the intensity of the response. As a result of these factors, nystagmus responses to caloric stimulation are highly variable and may fail to discriminate "normal" individuals from those with true pathology. Although Bárány had originally used angular accel-

erations and decelerations as a test of labyrinthine function, it has only been within the past few decades that fairly sophisticated and reliable torque-motor drive systems have made it possible to precisely control accelerations. The advent of laboratory minicomputers has also made it feasible to digitize and statistically analyze eye movement data in response to angular acceleration.

The present studies were predicated on research results employing the rhesus monkey as a model for responses to low-frequency harmonic (sinusoidal) acceleration. Data from these previous efforts^{3,4} showed that measures of the phase relationships between the input stimulus and the resulting eye movement output were highly repeatable and not influenced by changes in arousal level. It was also found that the sudden loss of a labyrinth (in this case by surgical destruction) could be detected by low-frequency harmonic acceleration and that the animals could not compensate for this loss, especially at the lower frequencies of stimulation.



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MATERIALS AND METHODS

Fifty-eight human subjects, ranging in age from 19 to 62 years, were tested. Each filled out a detailed questionnaire related to vestibular function; those with a history of inner ear problems were not included in the normal group. Eight sub-

jects with a history of labyrinthine pathology or a central nervous system disorder were given both caloric and rotational tests and their data included as case reports.

All subjects were sinusoidally accelerated about the vertical axis on a torque-motor (Contraves-Goerz, DP 300) turntable device. Maximum velocities were held constant at 50°/sec and the frequency varied over four octaves from .01 to .16 Hz. A few of the early tests were conducted by holding peak acceleration constant at 16°/sec² at each frequency. Data taken in this manner are identified appropriately in the figures. Eye movements were recorded by electro-oculographic techniques on an Offner type R dynograph and processed by an on-line analog and digital computer system. All tests were conducted in the dark with the subject's eyes open. During a five-minute

rest interval between each frequency, the subject was kept in red light illumination in an attempt to minimize changes in the corneoretinal potential. A number of question-and-answer tasks were employed to maintain the subject's level of arousal. Special analog and digital techniques were developed to analyze the peak slow-phase velocity, directional preponderance, and the phase relationships between the input acceleration and the resulting slow-phase eye velocity output.^{5,6}

RESULTS

Since some confusion exists regarding the exact nature of angular acceleration and its relationship to eye movements, a brief discussion of this is in order. As shown in Fig 1, acceleration results from a change in velocity over time. The slow-

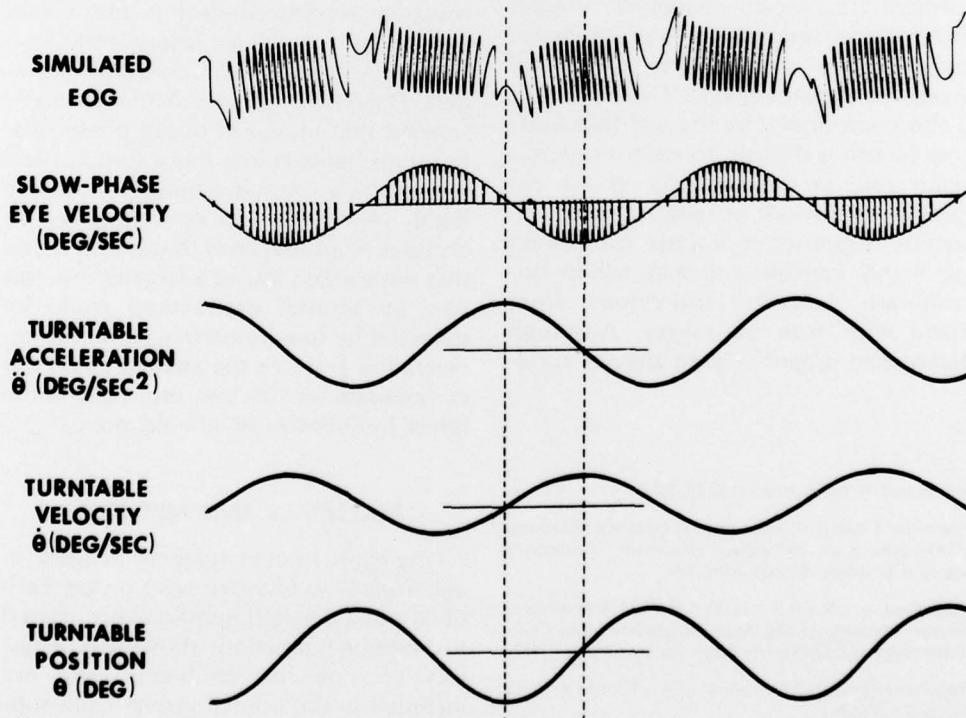


Fig 1.—Idealized acceleration input-output relationships.

phase eye movements in response to head displacement are compensatory; eg, when the head is displaced to the right, the eyes will deviate at the same velocity (if within the response range of the canals) to the left or 180° out of phase. This results in the slow-phase eye velocity leading acceleration by 90° and being 180° out of phase with velocity. However, this is typically the case only when the individual has combined visual and vestibular input. This combined visual-vestibulo-oculomotor reflex has a gain of one, ie, the eye moves at exactly the same velocity as the head but in the opposite direction. When the subject is deprived of visual input and has only vestibular information (the situation when acceler-

ated in the dark), there is a reduction in the gain; this varies as a function of both the period and intensity of the stimulus. There is also a decrement in the subject's ability to maintain the proper phase relationship to the acceleration as the period and intensity of the stimulus are varied.

The most encouraging aspect of the results of the present study was the repeatability of the phase measures. As shown in Fig 2, 17 of the subjects (chosen at random) were given repeat tests at intervals from one to ten weeks following their first exposure; none of the mean differences were significantly different from zero. The phase shifts at .02 and .04 Hz were the most reliable, while .16 Hz showed the greatest variability.

NORMAL SUBJECTS

N=17

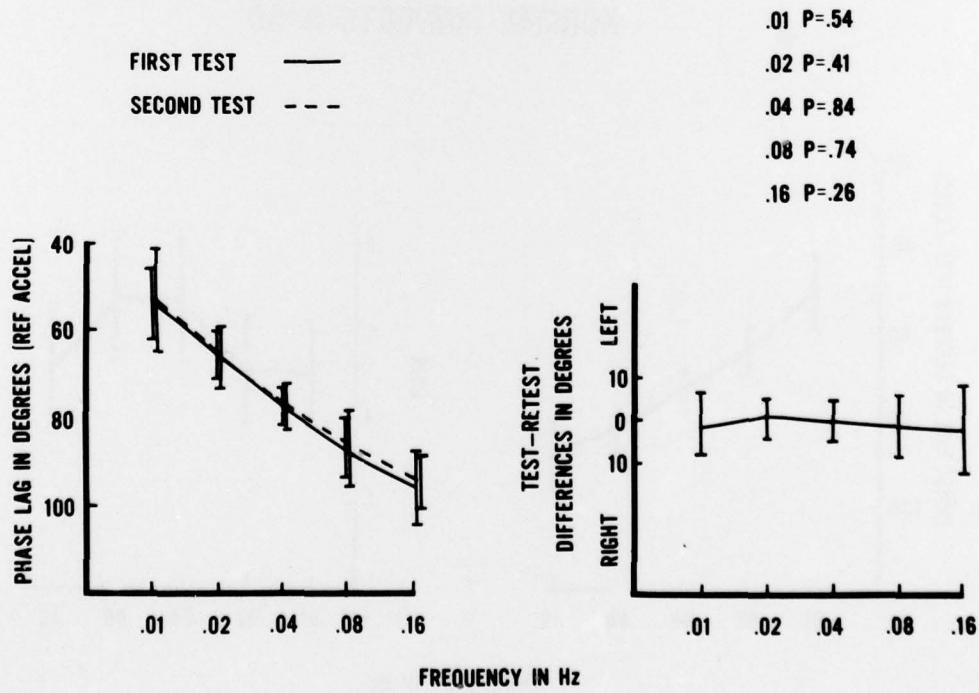


Fig 2.—Test-retest phase shift results from normal subjects as function of frequency.

Figure 3 shows the distribution of phase shifts and gains for the 50 normal subjects as a function of frequency. A test for normality indicated that the phase shift data were normally distributed at all five frequencies. Again, the midrange of the frequencies tested showed the least variability. The gain measures (output velocity/input velocity) were highly variable at all frequencies, and, although the gain showed an increase up to .04 Hz, there was an unexpected decrement at the highest frequency tested.

A measure of directional preponderance was also obtained by taking the ratio of $\frac{\text{Vel left} - \text{Vel right}}{\text{Vel left} + \text{Vel right}}$. The mean directional preponderance for the normal subjects was essentially zero at all fre-

quencies with a standard deviation of $\pm 10\%$; this variability was essentially the same for all frequencies tested (Fig 4).

CASE REPORTS

Based on these results, selected patients received both caloric and harmonic acceleration stimuli.

CASE 1.—A 25-year-old man had a history of chronic right ear infections from childhood; at age 19 he had mastoid surgery for this problem. Prior to surgery, hearing tests indicated that he was totally deaf in the right ear. Following surgery, the patient was left with a large mastoid bowl and was informed that his ear was completely "dead" on that side. We tested the patient six years postlabyrinthectomy and, as shown in Fig 5, he had no response to an air caloric on the right side. Harmonic acceleration reflected phase shifts at .01 and .02 Hz that approached 2 SD from the

PEAK VELOCITY $50^\circ/\text{sec}$
NORMAL SUBJECTS $N=50$

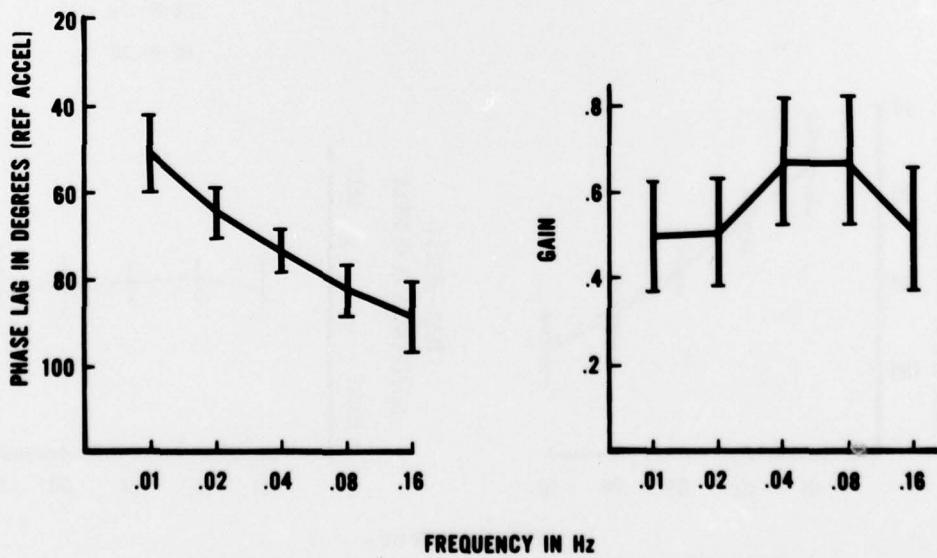
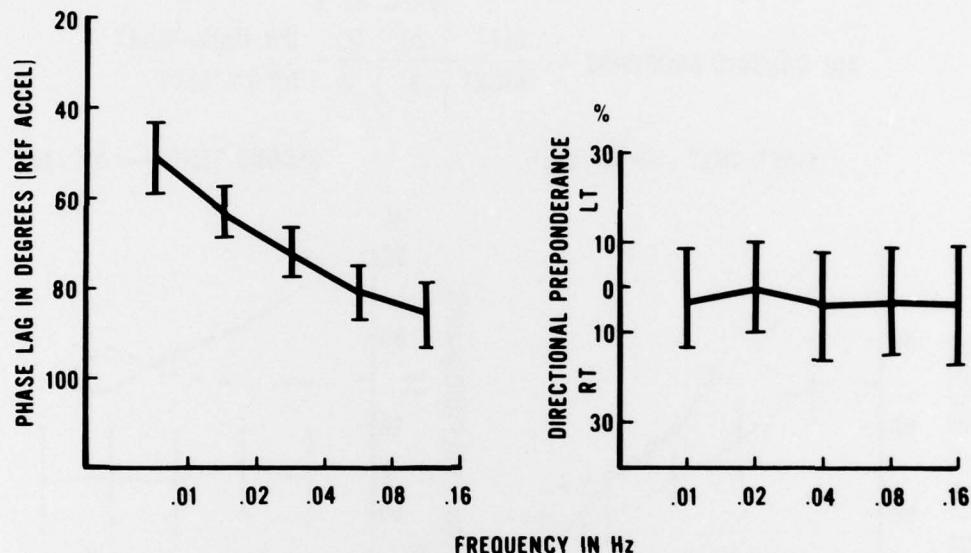


Fig 3.—Phase and gain measures from normal subjects (± 1 SD).

NORMAL SUBJECTS

N=50

Fig 4.—Phase and directional preponderance measures from normal subjects (± 1 SD).

normal mean and a directional preponderance to the left that was maximal (30% at .08 Hz). A repeat test of this patient two months later revealed almost identical phase shift results. Clearly, this patient's vestibulo-oculomotor system was unable to compensate for this peripheral deficit even though the loss had probably been gradual over the years.

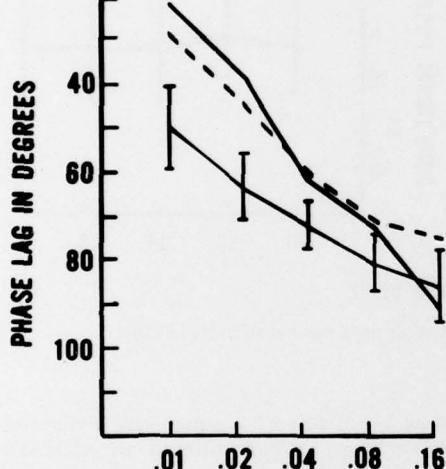
CASE 2.—A 26-year-old man was originally tested as part of our normal control group. However, analysis of this subject's phase shifts revealed responses that were over 2 SD from normal values at .01 Hz. He was retested and, again, almost identical results were obtained. These findings led to an extensive workup. It was found that he had double vision with left gaze and had been hospitalized for complete paralysis of the left side, supposedly related to migraine headaches and arterial spasm. He was diagnosed as having internuclear ophthalmoplegia, probably related to an infarction in the oculomotor complex. This patient also had a directional preponderance to the right during harmonic stimulation that was fairly uniform at all frequencies and agreed well with his unilateral weakness in response to caloric stimulation (Fig 6).

CASE 3.—A 62-year-old man was first tested 16 days after he had suffered an infarction clinically determined to be in the region of the left pontine brain stem anterior to the obex. Caloric testing indicated no response to cold water (30 C) in the left ear, even upon repeat testing. His phase shifts to harmonic acceleration were 1½ SD from the normal means at .01 and .02 Hz and were normal at .16 Hz (the highest frequency tested). He had a maximal directional preponderance of 16% to the right at .08 Hz (Fig 7). This patient was retested two months following his stroke: caloric testing revealed an inverted nystagmus with cold water in the left ear (fast-phase to the left) with a significant increase in response from the right ear with both cold and warm water. His phase lags to harmonic acceleration showed little change except at .08 Hz, which approached the normal mean value. Concomitantly, his directional preponderance, which had been greatest at .08 Hz, returned to normal at this frequency and he showed a marked increase in directional preponderance at .01 and .02 Hz, in agreement with his increased unilateral weakness based on caloric stimulation. It is important to note that his visual pursuit tracking had improved and he was also regaining

CASE 1

6 YEARS POST RIGHT LABYRINTHECTOMY

AIR CALORIC RESPONSE —			24°C	47°C	UW 100% RIGHT
	LEFT	RIGHT			
	20	21			
	0	0			DP 2% LEFT

FIRST TEST --- 16°/sec²

SECOND TEST — 50°/sec

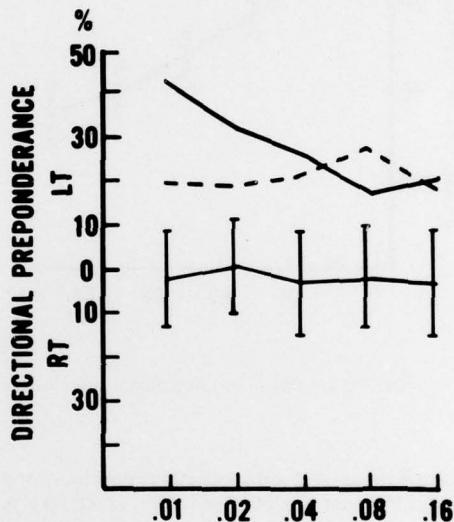


Fig 5.—Repeat test data at different acceleration levels: first test 16°/sec² at all frequencies; second test 50°/sec peak velocity (accel = $\frac{2\pi \text{ (vel)}}{\text{P (sec)}}$). Lower acceleration levels on second test show greater directional preponderance at .01 and .02 Hz (case 1).

some movement in his right side, which had been paralyzed.

CASE 4.—A 53-year-old man was first tested five days after suffering an infarction clinically determined to be located in the right brain stem at the pontine level. Caloric data revealed no response to cold water in the right ear and minimal nystagmic output in response to the remaining stimuli. This patient's responses to harmonic acceleration showed the greatest deficit at .04 Hz based on phase measures. He also reflected a severe weakness on the right side, as indicated by a marked directional preponderance at .02, .04, and .16 Hz (Fig 8).

CASE 5.—A 46-year-old man was diagnosed as suffering from Meniere's disease on the

right. His caloric test indicated a unilateral weakness of 34% on the right and a directional preponderance to the left of 24%; rotational testing indicated a maximal directional preponderance to the left of 25% at .02 Hz. This patient's phase shifts reflected values that were below the normal mean values at the lower frequencies with a crossing-over at .04 Hz and then well above the normal mean at .08 Hz (Fig 9). The patient was in remission at the time of testing.

CASE 6.—This patient (Fig 10) was also diagnosed as having Meniere's disease but on the left side. This patient's phase shift showed the same pattern as case 5, with a reversal in the directional preponderance (to the right) that was maximal between .02 and .04 Hz.

CASE 2

INTERNUCLEAR OPHTHALMOPLEGIA

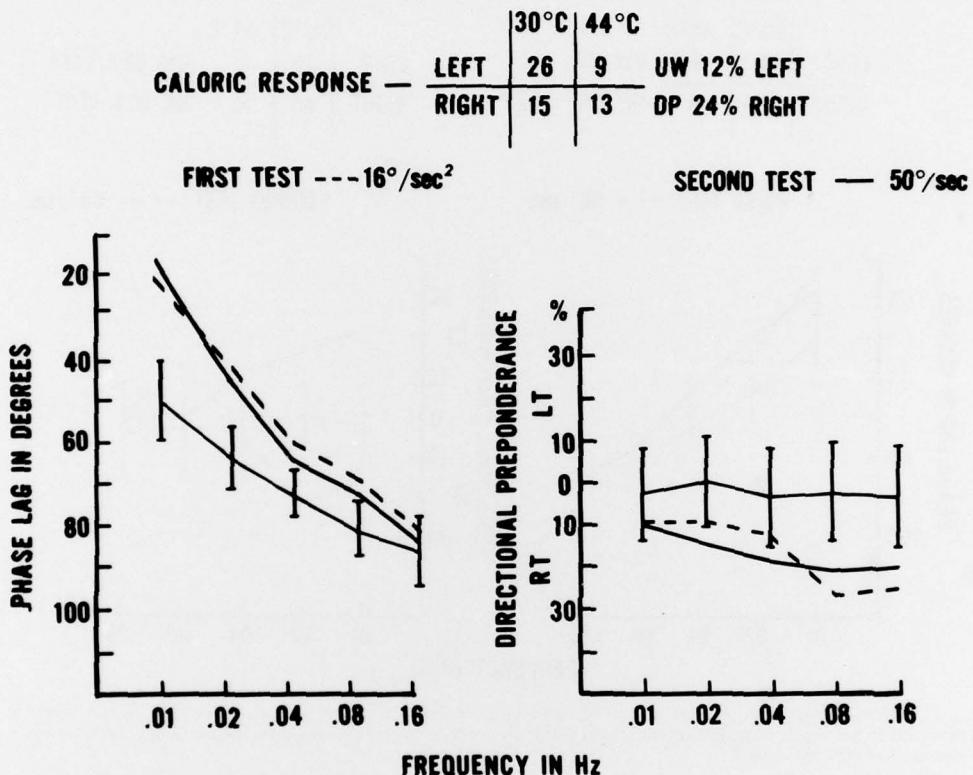


Fig 6.—Repeat test data (from patient with oculomotor lesion) at different acceleration levels (case 2).

CASE 7.— A 28-year-old man who had a history of dizziness and vertigo complained of symptoms at the time of testing. His caloric responses were within normal limits, and his slow-phase output in response to acceleration was also normal. However, his phase shifts with reference to acceleration were 1 SD from the normal mean at .02 and .01 Hz (Fig 11), indicating that his symptoms were probably related to a minimal peripheral deficit that was not revealed by caloric testing.

CASE 8.— A 57-year-old man was diagnosed as having diffuse cerebellar degeneration related to chronic alcohol abuse; he complained of dizziness and subjective vertigo. His caloric responses showed almost perfect symmetry; however, harmonic acceleration revealed a directional preponderance to the left that in-

creased to a maximum of 25% at .16 Hz. His phase shifts were normal at the higher frequencies but showed an increase in impairment as the frequency decreased below .04 Hz (Fig 12). This case is clearly one in which harmonic acceleration was a more sensitive test of the vestibulo-oculomotor system.

DISCUSSION

As mentioned above, one of the most promising results of the present study was the repeatability of the phase measures of the slow-phase eye movements to acceleration. This is obviously related to the fact that the input stimulus (acceleration) can be precisely controlled and the phase

CASE 3

INFARCTION LEFT PONTINE BRAIN STEM

	30°C	44°C	
LEFT	0	9	UW 56% LEFT
RIGHT	13	19	DP 8% LEFT

	30°C	44°C	
LEFT	-5	8	UW 92% LEFT
RIGHT	45	30	DP 36% LEFT

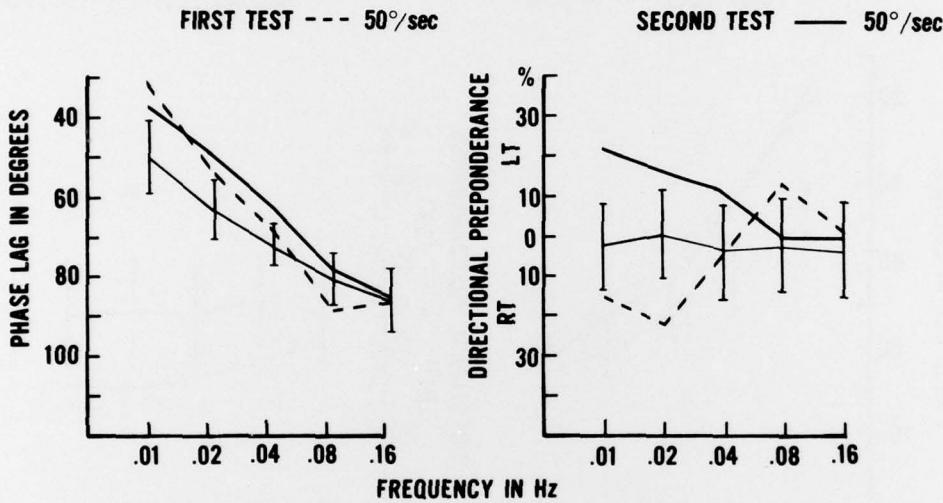


Fig 7.—Repeat tests from patient indicating greater deficit of caloric response on second test. However, responses to harmonic acceleration indicated some recovery of function that agreed more closely with patient's improved condition (case 3).

measures appear to be independent of arousal level. The variability in the gain of the response is undoubtedly related to variations in arousal, which are difficult to control even with mental tasks. The fact that the gain does not increase predictably with increasing frequency is not surprising; one should not expect the eye movement response to agree with the linear system model that has been developed for the semicircular canals since a great deal of neural interaction occurs between the cupula and the final eye movement output.

Another important factor that is frequently overlooked in linear system analysis is that the semicircular canals are paired structures which are actually

asymmetric in neural output. As Ewald⁵ pointed out in 1892, utriculopetal movement of the cupula is a more adequate stimulus than utriculofugal deflection. This was especially evident in our previous studies of animals with a unilateral labyrinthectomy: utriculopetal stimulation of the intact labyrinth produced almost twice the slow-phase velocity as did utriculofugal movement. This is probably related to the fact that utriculopetal deflection leads to a depolarization of hair cells and an increase in neural discharge, whereas utriculofugal movement causes most of the hair cells to hyperpolarize with a decrease in cell firing. Although cell discharges can increase in frequency up to the refractory period of

CASE 4

INFARCTION RIGHT PONTINE BRAIN STEM

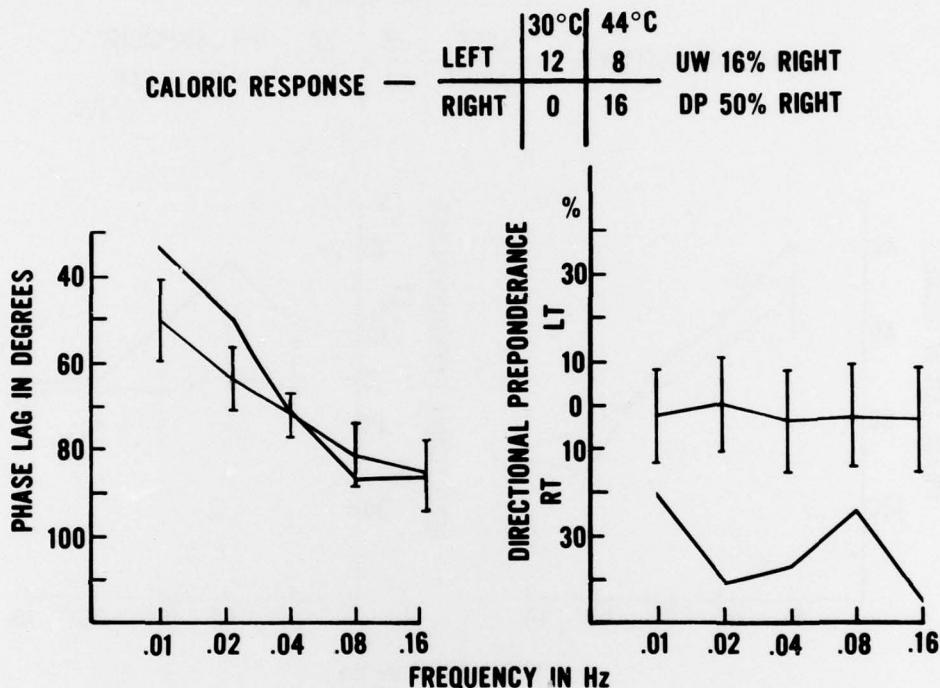


Fig 8.—Data from patient with central lesion showing marked changes in directional preponderance as function of frequency (case 4).

the axon (1,000/sec), the cell can only decrease from its resting level to zero. This situation, by definition, leads to an end-organ response that is asymmetric. If this were not true, it would be impossible (as many still believe) to use rotation to test a single end-organ, ie, one ear. However, only in a normal system with both ears operating as a synergistic pair can one obtain perfect symmetry. Therefore, any impairment of a canal system, especially with utriculopetal deflection, will be detected as a decrement in response of either total slow-phase output or the phase relationship between the input and the output. This interpretation is also supported by the few case studies which

we have included; the directional preponderance and unilateral weakness as indicated by caloric testing were in agreement with the directional preponderance in response to harmonic acceleration, and the responses to acceleration appeared to be a more sensitive measure of directional preponderance. It should be noted that the concept of directional preponderance is inconsistent with linear systems theory: bilateral linear systems, by definition, have no directional preponderance. Thus, attempts to analyze the vestibular system in the presence of unilateral dysfunction by linear theory yield an incomplete system description. Some measure of system asymmetry (such

CASE 5

MENIERE'S DISEASE (RT)

CALORIC RESPONSE	30°C		44°C		UW 34% RIGHT
	LEFT	16	RIGHT	8	
	13			8	DP 24% LEFT

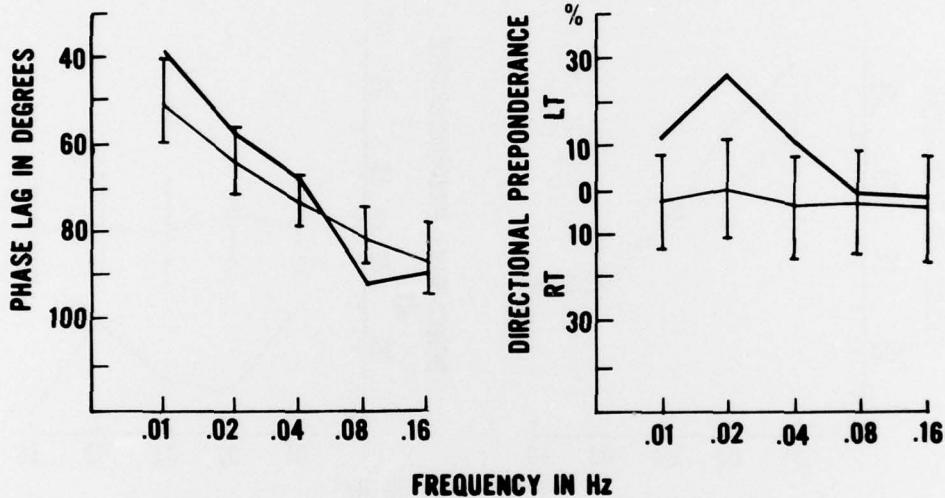


Fig 9.—Patient with right Meniere's disease; directional preponderance at .02 Hz agrees with that revealed by caloric testing. Phase shifts cross from a lag to a lead as function of frequency (case 5).

as directional preponderance) should be included to supplement the linear measures of gain and phase.

The finding that one cannot compensate for permanent impairments in the vestibulo-oculomotor reflex further enhances the clinician's ability to determine if the individual's pathology is undergoing a change. In those individuals with stable conditions, retest results were within a few degrees of their original responses. In those patients in which there was a change in condition, this was reflected in a change in their responses to harmonic acceleration.

At present it is not known which parameters are best for assessing vestibulo-oculomotor function with harmonic acceleration. Pilot studies in our laboratory indicate that acceleration levels (8 to $32^{\circ}/\text{sec}^2$) have little effect on the phase shifts but do cause changes in the directional preponderance: the higher levels of acceleration (above $25^{\circ}/\text{sec}^2$) appear to lead to a more symmetric response. This is evident in the responses from cases 1 and 2. Our original studies had been designed to hold acceleration constant at $16^{\circ}/\text{sec}^2$ and these two patients were first tested at these parameters. However, for a number of technical reasons, we

CASE 6

MENIERE'S DISEASE (LT)

CALORIC RESPONSE —	30°C		44°C	
	LEFT	RIGHT	LEFT	RIGHT
	48	13	UW 6% LEFT	
	33	22	DP 20% RIGHT	

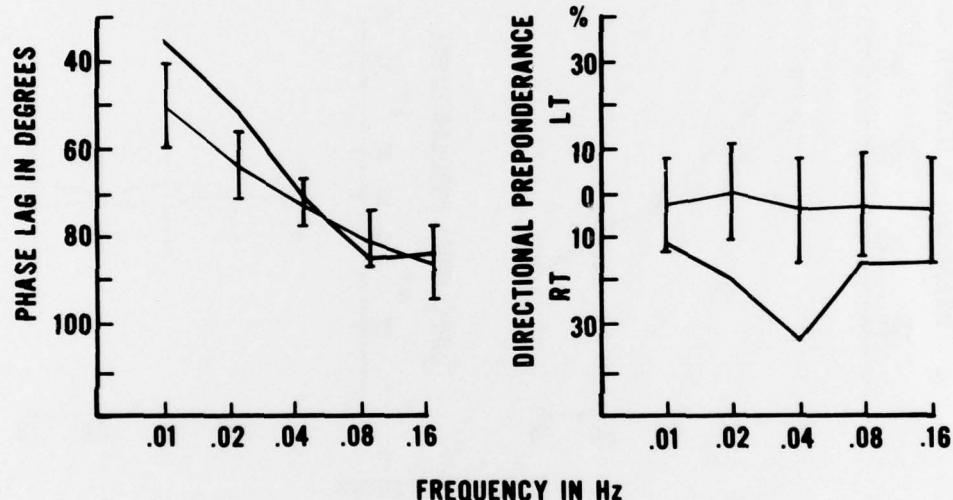


Fig 10.—Patient with left Meniere's disease (case 6). Data are similar to Fig 9 but reversed in directional preponderance; greatest deficit in directional preponderance occurred at .04 Hz.

changed the test by limiting angular velocity to a maximum of $50^{\circ}/\text{sec}$ at all frequencies; as a result, acceleration values were lowered to $3^{\circ}/\text{sec}^2$ at 0.01 Hz and increased to a maximum of $50^{\circ}/\text{sec}^2$ at 0.16 Hz .⁴ This indicates that acceleration should perhaps be held constant at an intensity below $25^{\circ}/\text{sec}^2$ and velocity allowed to vary. In earlier studies in our laboratory, Mathog,⁶ in 1972, found that with constant acceleration ($23^{\circ}/\text{sec}^2$) the directional preponderance was similar to the results of caloric tests at the midfrequency ($.08\text{ Hz}$) and showed distortion at higher frequencies. It is fairly obvious from our studies that the lower frequencies of stimulation (below $.04\text{ Hz}$)

are more sensitive in detecting abnormalities reflected in phase shifts. It appears that even lower frequencies than $.01\text{ Hz}$ may be useful in detecting abnormalities in the vestibulo-oculomotor system, and we intend to evaluate $.005\text{ Hz}$ as a stimulus.

SUMMARY

These preliminary findings reveal that low-frequency harmonic acceleration can be used to detect unilateral peripheral deficits that agree with caloric findings. However, the responses to sinusoidal acceleration are less variable than the caloric responses and allow one to more

CASE 7

HISTORY OF DIZZINESS AND VERTIGO

CALORIC RESPONSE —	30°C		44°C	
	LEFT	34	22	UW 12% LEFT
RIGHT	40	32	DP 4% RIGHT	

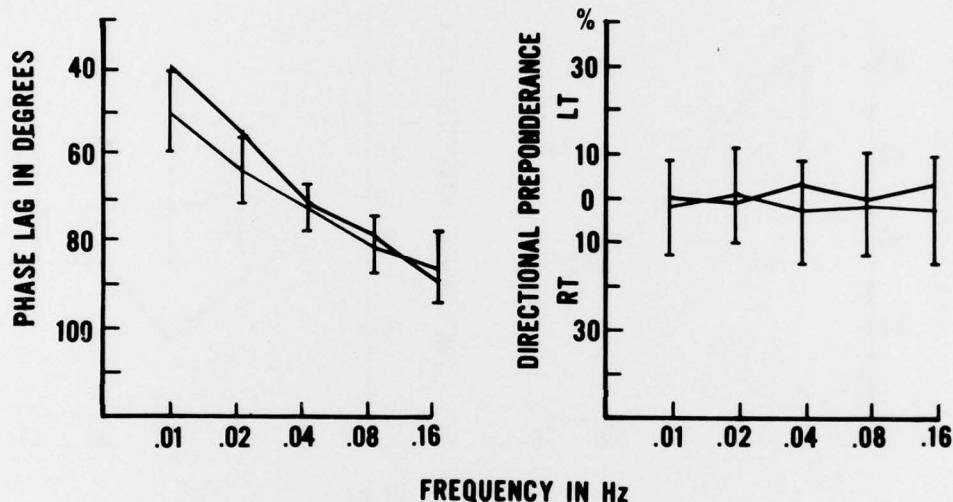


Fig 11.—Data reflect normal caloric response and no significant directional preponderance on harmonic; however, phase shifts show partial decrement at lower frequencies (case 7).

closely evaluate changes in pathology with time. Therefore, it appears that harmonic acceleration provides additional information that is useful in confirming other test results and that a complete otoneurologic evaluation should include this type of rotational testing.

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The voluntary informed consent of the subjects used in this research was obtained in accordance with AFR 80-33.

Key Words: Vestibular; harmonic stimulation; acceleration; normal humans; clinical cases.

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CASE 8

DIFFUSE CEREBELLAR DEGENERATION

CALORIC RESPONSE -			30°C	44°C
	LEFT	RIGHT		
	13	17		UW 4% LEFT
	19	13		DP 4% LEFT

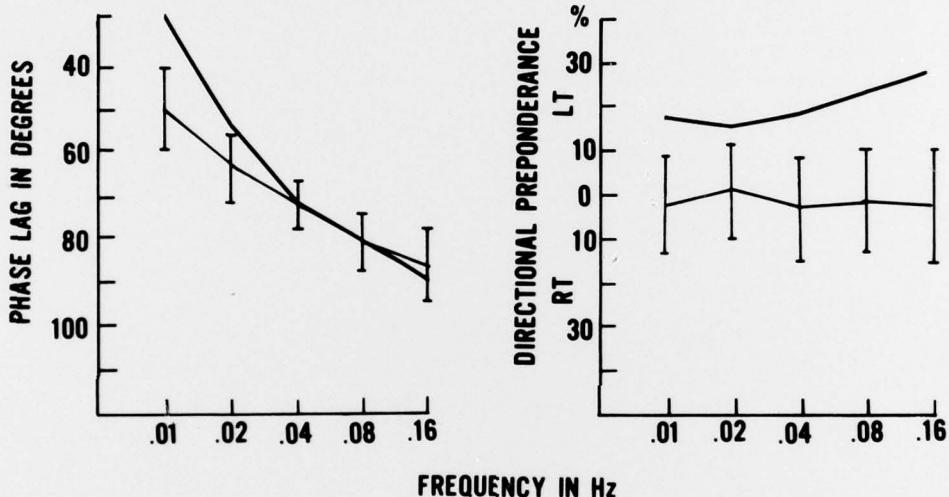


Fig 12.—Data reflect normal caloric response but considerable directional preponderance on harmonic acceleration and decrement in phase lag below .04 Hz (case 8).

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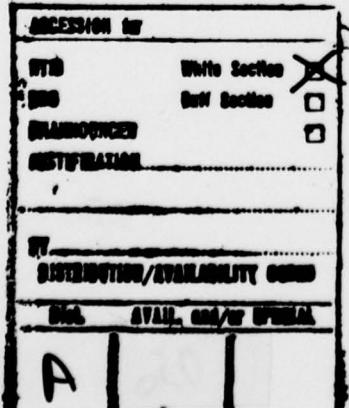
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